REMARKS

Claims 99-112 are now pending. Claims 89-98 and 102-104 have been withdrawn from consideration by the Examiner. Claims 89-98 have been cancelled by this amendment. New claims 105-112 are submitted for consideration. The following remarks are directed to pending claims 99-101 and 105-112. The claims present methods for computationally manipulating character strings that represent potential compositions of matter (polynucleotides and/or polypeptides). The character strings are not themselves compositions of matter.

Support for the amendment to claim 99 and for the new claims is found throughout the specification and in the originally submitted claims. For example, original claim 1 and its dependent claims 21 and 26 support the new features recited in claim 99. As another example, new claim 105 finds support in original claim 1 and its dependent claims 21 and 25. Further new claims 108 and 110 find support at page 6, lines 8-11. And new claims 109 and 111 find support at page 42, line 15 TO page 43, line 13.

Claims 99-101 were rejected under 35 USC 103 as being unpatentable over the combination of Venkatasubramanian et al. (J. Chem. Inf. Comput. Sci., Vol. 35, pp. 188-195) in view of US Patent No. 6,403,312 issued to Dahiyat et al. It is respectfully submitted that these references fail to disclose or suggest certain features of the pending independent claims.

Venkatasubramanian et al. describes a genetic algorithm for identifying a repeat unit of an industrial polymer such as polyethylene terephthalate (PET), polyvinylidene propylene copolymer, polycarbonate of bisphenol-A, and the like. In the genetic algorithm, various mainchain groups (>C<, -S-, -O-(C=O)-, -NH-, -(C=O)-NH-, phenyl based groups, complete monomer units, etc.) and sidechain groups (-H, $-CH_3$, -Cl, -CN, $-O-(C=O)-OCH_3$, etc.) are brought together to create the repeat units under consideration. These mainchain and sidechain groups are present in seed population, and are manipulated to produce next generation repeat units by applying various *operators* identified at page 190. Crossover is among the operators used by Venkatasubramanian in their study. A fitness function selects particular repeat units in each generation to be used in a succeeding generation. The fitness function selects on the basis of various materials properties such as density, glass transition temperature, thermal expansion coefficient, specific heat capacity, and bulk modulus. See page 191, left column.

Various features of the pending claims that are not employed in the Venkatasubramanian et al. genetic algorithm. For example, the Venkatasubramanian et al. algorithm does not select a crossover point on the basis of pairwise homology (either from a region of identified pairwise homology (claim 105) or from a region outside of an identified pairwise homology region (claim 99)). In addition, the Venkatasubramanian et al. genetic algorithm is not concerned with nucleotide or peptide applications. Therefore, its character strings do not represent "one or more polynucleotides or polypeptides" and it does not computationally select "a set of character substrings having sequences that identify the set of oligonucleotides for *in vitro* recombination." Both of these features are recited in the independent claims.

The Examiner has cited the patent to Dahiyat et al. for "teaching of making novel proteins or nucleic acids by recombination or mutation." As an example, the Examiner points to the Dahiyat et al. procedure for making and computationally screening an array of mutant polypeptides of β-lactamase TEM-1.

Generally, the Dahiyat et al. patent describes a computational method of introducing diversity in a "scaffold" peptide sequence by identifying specific amino acid residues for variation. The starting point for the process is a single "scaffold" sequence. Column 5, line 16 to column 6, line 46. Mutations in this scaffold at the identified residues are selected for a "primary library." Column 6, line 47 to column 14, line 39. Then combinations of these mutations are provided in various sequences to generate a secondary library. Column 14, line 40 to column 16, line 28. Each of these steps, including generation of the secondary library is performed computationally. Dahiyat et al. describe no other computational techniques of relevance.

It is respectfully submitted that Dahiyat et al. does not suggest a computational crossover operation – as "crossover" is conventionally understood in the art. But regardless of how the term "crossover" is interpreted, the Dahiyat et al. patent clearly fails to suggest selecting a crossover point on the basis of pairwise homology. And, even if it did, it does not suggest certain claimed features of the computationally selected set of oligonucleotides for *in vitro* recombination. For example, it does not suggest that the set include "at least one oligonucleotide comprising a chimeric nucleic acid sequence that comprises subsequences from at least two of the parental character strings." Fundamentally the concept of a chimeric sequence comprised of subsequences from two parent sequences and joined at a crossover point is lacking in the Dahiyat et al. patent.

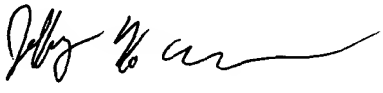
New independent claim 112 is similar to pending claims 99 and 105, but does not recite a separate alignment operation or a selecting a crossover point based on homology considerations. Thus, claim 112 is broader in some regards than claims 99 and 105. Nevertheless, it is believed that this claim is patentable over the art of record. As indicated, neither the Venkatasubramanian et al. paper nor the Dahiyat et al. patent suggest, for example, identifying an "oligonucleotide comprising a chimeric nucleic acid sequence that comprises subsequences from at least two of the parental character strings."

For the reasons set forth above, it is respectfully submitted that claims 99-101 and 105-112 are allowable over the combination of the Venkatasubramanian et al. paper and the Dahiyat et al. patent. Applicants respectfully request a Notice of Allowance for this application.

As a final matter, it is noted that the Examiner has refused to examine the claims of groups II and III together. According to the Examiner, "the methods of identifying nucleic acids and a computer system have certainly acquired a separate status in the art as a separate subject for inventive effect and are usually published separately." Applicants understand and respect this position, but respectfully disagree. It is certainly inconsistent with the great majority of similar cases encountered by the undersigned representative in prosecuting both bioinformatics method claims and corresponding "Beauregard" claims. (Note that Beauregard or "computer program product" claims are not normally viewed as computer systems, but rather as memory or other media on which instructions for carrying out a method are stored.) In numerous cases, the undersigned has not previously encountered an examiner who has issued and maintained a restriction between method and corresponding Beauregard claim groups. Applicants recognize that examination decisions by one PTO examiner are not used as precedent for other examinations. Nevertheless, Applicants felt that the Examiner might be interested in this information.

Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set out below.

Respectfully submitted,
BEYER WEAVER & THOMAS, LLP



Jeffrey K. Weaver
Reg. No. 31,314,

P.O. Box 778
Berkeley, CA 94704-0778
(510) 843-6200